

REMARKS

Claims 49, 57, 58 and 79-81 are pending in the subject application, with claims 1-48, 50-56 and 59-78 having previously been canceled, without prejudice or disclaimer. By this Amendment, claim 49 has been amended to clarify the claimed subject matter. Support for the claim amendment can be found in the application as originally filed, for example, at page 13, line 35 through page 14, line 3, page 34, lines 7-20, and page 52, line 10 through page 53, line 15. Accordingly, Applicant respectfully requests that this Amendment be entered. Claims 49, 57, 58 and 79-81 remain pending upon entry of this amendment, with claim 49 being the sole pending claim in independent form.

Rejections Under 35 U.S.C. § 103(a)

In section 3 of the January 6, 2011 Office Action, claims 49, 57, 58 and 79-81 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hollis et al. (US 5,846,708) in view of Cozzette et al. (US 5,063,081).

Applicant respectfully submits that the present application is allowable over the cited art, for at least the reason that the cited art does not disclose or suggest various aspects of the present application such as a method for analyzing a sample oligonucleotide sequence in solution comprising **controlling a level of stringency of hybridization, by adjusting a power level of said electric field and/or a length of time said individually selected microlocations are subjected to said electric field** in step (f), to improve said analyzing of the sample oligonucleotide sequence, by enabling removal of partially hybridized sequences and improving the resolution of single mis-match hybridizations.

As discussed in the present application, the outcome of

hybridization can be perfect-match hybrids or hybrids including varying degrees of mismatches, depending on the hybridization conditions. The ability to control the stringency of the hybridization facilitates hybridization specificity, and it is particularly important for resolving one base mismatches in point mutations, as explained, for example, on page 34, lines 7-26 of the present application. Control of stringency also allows, by adjusting the hybridization conditions, to achieve a desired degree of hybridization specificity, including a desired number of mismatches.

As discussed on page 52, lines 15-17 of the present application, stringency control is performed conventionally by varying salt concentration (ionic strength) and temperature.

On the other hand, in the aforementioned aspects of the present application, control of the stringency of hybridization is performed by electronic means, for example, by adjusting the length of time the microlocations are subjected to an electric field in step (f), following hybridization, and/or by adjusting the power level of the electric field. Figure 11 and the corresponding description on page 34, lines 7-26 demonstrate electronic control of hybridization for resolving a single base mismatch by delivering a defined amount of power following the hybridization, in order to denature and remove the mismatched DNA hybrids while retaining the perfectly matched hybrids. Additionally, example 9 on page 52, line 10 through page 53, line 15 of the present application explains that the stringency of hybridization with sequences including 0-2 mismatches can be affected by the electrophoretic potential applied.

Both Hollis and Cozzette are completely silent regarding

electronic control of the stringency of hybridization, as claimed in the present application.

Indeed, Cozzette does NOT discuss the issues of stringency control or mismatches in hybridization at all.

Hollis, column 14, lines 10-13, proposes that "a reverse biased potential can be subsequently applied to aid in the washing (removal) of unhybridized and mismatched target molecules", and Hollis, column 6, lines 45-48, proposes that "some weakly bound target mismatches may occur, *but these can be alleviated by rinsing the well with an appropriate solution at an appropriate ion concentration and temperature*".

However, Hollis does NOT address the issue of **controlling stringency** of the hybridization (that is, the number of permitted mismatches), to resolve single base mismatches or to allow varying degrees of mismatches. Moreover, while Hollis suggests reversing the potential in order to remove unhybridized and mismatched target molecules, Hollis does NOT teach or suggest adjusting the power level of the electric field or the length of time the electric field is applied in order to **control the stringency of hybridization**.

Applicant submits that a person of ordinary skill in the art at the time of the invention of Hollis would NOT be motivated to adjust the power level or length of application of the electric field in order to control the stringency of the wash, since the methods known in the art for this purpose, as suggested in Hollis, column 6, lines 45-48, include varying ionic strength and temperature.

Applicant submits that the cited art, even when considered along with common sense and common knowledge to one skilled in the art, simply does **NOT** render unpatentable the aforementioned aspects of the present application of a method for analyzing a sample oligonucleotide sequence in solution comprising **controlling a level of stringency of hybridization, by adjusting a power level of said electric field and/or a length of time said individually selected microlocations are subjected to said electric field** in step (f), to improve said analyzing of the sample oligonucleotide sequence, by enabling removal of partially hybridized sequences and improving the resolution of single mis-match hybridizations.

Accordingly, applicant submits that amended claim 49 and the claims depending therefrom are allowable over the cited art.

In view of the remarks hereinabove, applicant maintains that the application is now allowable. Accordingly, applicant earnestly solicits the allowance of the application.

However, if the Examiner can suggest an amendment that would advance this application to condition for allowance, the Examiner is respectfully requested to call the undersigned attorneys.

If a petition for an extension of time is required to make this response timely, this paper should be considered to be such a petition.

No fee, other than the \$405.00 Request for Continued Examination fee and the \$65.00 one-month extension of time fee, are deemed necessary in connection with the filing of this Amendment. However, if any further fees are required, authorization is

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Filed: July 22, 1999
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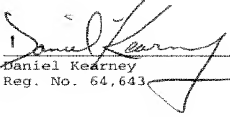
hereby given to charge the amount of any such required fee to
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Respectfully submitted,



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This correspondence is being filed
electronically with the U.S. Patent
and Trademark Office via EFS-Web.



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May 6, 2011

Date